

Appl. No. 10/004,800  
Amdt. Dated Jun. 26, 2003  
Reply to Office action of Feb. 26, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (original): A spectrometer comprising:

an ion mobility spectrometer (IMS) device, for use in promoting separation of ions based on different mobility characteristics, the ion mobility spectrometer device comprising:

an inlet for ions;

an ion mobility section for receiving ions from the ion inlet;

~~and~~ means for forming an axial DC field within the ion mobility section, to generate a potential gradient along the axis thereof;

a1 ~~and~~ means for maintaining a gas at a desired pressure within the mobility section, whereby ions traveling through the mobility section under the influence of potential gradient are subject to collision with the gas, promoting separation based on differing mobility characteristics;

~~an ion focusing section for receiving ions from the ion mobility section, and including an RF ion guide having an axis, and means for supplying an RF voltage to the RF guide, to generate a field to promote focusing of ions along the axis of the RF ion guide, the ion mobility section being one of upstream from and integral with the ion focusing section ; and~~

at least one mass analysis section, providing a final mass analysis section, for receiving ions from the RF ion guide and for separating ions based on differing mass-to-charge characteristics.

Claim 2 (original): A spectrometer as claimed in claim 1, wherein said means for maintaining a gas pressure comprises a gas supply, mounted for supplying gas to the mobility section, for maintaining a desired pressure in the mobility section.

Claim 3 (original): A spectrometer as claimed in claim 1, which includes means for forming an axial DC field along the RF ion guide, to generate a potential gradient therealong to enhance movement of ions through the RF ion guide.

Claim 4 (original): A spectrometer as claimed in claim 1, wherein the ion mobility section includes at least one of: a ring guide including a plurality of rings arranged spaced apart and around the axis thereof; a multipole rod set comprising a plurality of rods arranged around the axis thereof; and a conductive cylinder with the axis of the ion mobility section extending down the axis of the cylinder.

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Claim 5 (original): A spectrometer as claimed in claim 4, wherein the RF ion guide comprises at least one of: a ring guide including a plurality of rings arranged spaced apart and around the axis of the RF ion guide; and a multipole rod set comprising a plurality of rods arranged around the axis of the RF ion guide.

Claim 6 (original): A spectrometer as claimed in claim 4 or 5, wherein the RF ion guide comprises a multipole rod set arranged around the axis thereof and wherein each rod comprises a plurality of rod segments, and wherein the ion focusing section includes a power supply for a DC voltage, connected to the rod segments, for supplying different DC voltages to the rod segments, thereby to generate the DC field and a potential gradient along the axis of the rod set.

Claim 7 (original): A spectrometer as claimed in claim 6, wherein the power supply is switchable to supply voltages to the rod segments whereby a plurality of potential wells are formed.

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Claim 8 (original): A spectrometer as claimed in claim 1, 2, 3, 4 or 5, which includes means for forming a DC field and a potential gradient along the axis of the ion focusing section, said means comprising one of: auxiliary elements located around the rod set and connected to a power supply for generating the DC field and the potential gradient; a multipole rod set arranged around the axis of the RF ion guide, with the rods of the multipole rod set having inclined surfaces whereby a potential gradient can be formed.

Claim 9 (original): A spectrometer as claimed in any one of claims 1 to 5, wherein said means for maintaining a gas pressure maintains a pressure of approximately 760 Torr in the ion mobility section.

Claim 10 (original): A spectrometer as claimed in any one of claims 1 to 5, which includes an ion source comprising one of: an electrospray ion source and a MALDI source.

Claim 11 (original): An apparatus as claimed in claim 1, wherein the ion mobility section includes a multipole rod set provided as a plurality of rod segments axially aligned with one another, a first voltage supply means connected to the rod segments for supplying an RF voltage, for focusing ions, and a second voltage supply for supplying DC voltages, connected to the rod segments for generating, in use, a potential gradient through the ion mobility section.

Claim 12 (original): An apparatus as claimed in claim 11, wherein the final mass analysis section comprises a time-of-flight mass analyzer.

Claim 13 (original): An apparatus as claimed in any one of claims 1 to 5, which includes a first mass analysis section and a collision cell provided between the ion focusing section and the final mass analysis section.

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Claim 14 (original): An apparatus as claimed in claim 13, wherein the first mass analysis section comprises a quadrupole mass analyzer and wherein the collision cell includes a quadrupole rod set.

Claim 15 (original): An apparatus as claimed in claim 14, wherein the quadrupole rod set of the collision cell is provided as a plurality of rod segments, and wherein a power source is provided connected to the rod segments of the collision cell quadrupole rod set, for generating an axial DC field there along.

Claim 16 (original): A method of separating ions based on ion mobility characteristics, the method comprising:

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- (i) generating ions;
  - (ii) providing at least one drift region having an axis extending therealong and providing and maintaining a gas at a desired pressure in the drift region;
  - (iii) forming a DC potential gradient along the drift region;
  - (iv) supplying ions to the drift region, whereby ions are driven through the drift region by the potential gradient and ions tend to separate due to differing ion mobility characteristics;
  - (v) passing the ions through an RF ion guide and maintaining gas at a pressure in the RF guide sufficient to focus the ions along an axis of the RF ion guide; and
  - (vi) passing ions into a mass analyzer for mass analysis in dependence upon ion mass-to-charge ratios.

Claim 17 (original): A method as claimed in claim 16, which includes adjusting parameters of at least one of the mass analyzer and the drift region to follow changes in properties of the ions eluting from the drift region.

Claim 18 (original): A method as claimed in claim 17, which includes separating ions into groups of ions in step (iv) in dependence upon ion mobility characteristics, and sequentially analyzing each group of ions in step (vi).

Claim 19 (original): A method as claimed in claim 16, 17 or 18, which includes mass analyzing the ions in step (vi), with a time-of-flight mass spectrometer.

Claim 20 (original): A method as claimed in claim 18, which includes establishing for each group of ions an approximate range of mass-to-charge ratios present in the group, and mass analyzing the ions in step (vi) in a Time-of-Flight mass analyzer,

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and setting timing of the Time-of-Flight mass analyzer in dependence upon the range of mass-to-charge ratios present in each group, thereby to enhance the sensitivity of mass analysis in the Time-of-Flight mass analyzer.

Claim 21 (original): A method as claimed in claim 18 or 20, wherein all of the groups of ions together encompass all of the ions eluting from the ion mobility section within a desired range of mass-to-charge ratios.

Claim 22 (original): A method as claimed in any one of claim 16, 17, 18 or 20, which includes, for step (v), passing ions from the drift region into a multipole rod set, providing the RF ion guides and providing an RF signal to the multipole rod set, to cool and focus the ions along an axis of the rod set, wherein the method further comprises adjusting at least one of the frequency and the amplitude of the RF to follow variations in mass-to-charge ratios of ions eluting from the drift region.

Claim 23 (original): A method as claimed in claim 16, which includes, between steps (v) and (vi), passing the ions through a collision cell to promote formation of product ions; by one of fragmentation and reaction, and subsequently mass analyzing the product ions in step (v).

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Claim 24 (original): A method as claimed in claim 23, which includes, before passing ions into the collision cell, subjecting the ions to an upstream mass analysis step, to select a desired precursor ion for said at least one of fragmentation and reaction, and periodically resetting the precursor ion selected in said upstream mass analysis step, as different ions elute from the RF ion guide in step (iv), thereby to increase usage of ions from a sample.

Claim 25 (original): A method as claimed in claim 16, 17 or 18, which includes controlling flow of ions from the ion mobility spectrometer with a gate, and adjusting the potential on the gate to either permit passage of ions or prevent passage of ions.

Claim 26 (original): A method as claimed in claim 16, which includes providing the RF ion guide as a multipole rod set comprising a plurality of rod segments providing different DC potentials to axially spaced rod segments, and the method further comprising:

- (a) receiving ions from the drift region and initially applying a uniform potential gradient along the rod set;
- (b) after ions are uniformly distributed along the length of the rod set according to their mobility, establishing a potential well structure to retain groups of ions in separate potential wells; and
- (c) releasing ions separately from each potential well for subsequent mass analysis.

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Claim 27 (original): A method as claimed in claim 26, which includes providing all or part of the drift region within the multipole rod set.

Claim 28 (original): A method as claimed in claim 26 or 27, which includes reducing the gas pressure after establishing the potential wells, to increase ion life time in the potential wells.

Claim 29 (original): A spectrometer comprising: an ion mobility spectrometer device, for use in promoting separation of ions based on different mobility characteristics, the ion mobility spectrometer device comprising

an inlet for ions;

a drift region;

means for forming a DC field along the drift region, to generate a potential gradient along the drift region; and means for maintaining a gas pressure within the drift region, whereby ions traveling through the drift region under the influence of a potential gradient are subject to collision with a gas, promoting separation based on differing ion mobility characteristics;

a collision cell connected to the ion mobility spectrometer for receiving ions therefrom and including a gas therein, for promoting at least one of fragmentation of ions and reaction of the ions with ambient gas, to form product ions;

an RF ion guide having an axis, and means for supplying an RF voltage to the RF guide, to generate a field to promote focusing of ions along the axis of the RF ion guide, and

a final mass analysis section for analyzing the product ions received from the RF ion guide.

Claim 30 (original): A spectrometer as claimed in claim 29, which includes a first, mass analysis section between the ion mobility spectrometer and the collision cell, whereby the final mass analysis section comprises a second mass analysis section.

Claim 31 (original): A spectrometer as claimed in claim 30, wherein the ~~ion mobility spectrometer includes~~ RF ion guide comprises at least one of:

(i) a ring guide section comprising a plurality of axially aligned rings and a power supply connected to the rings for generating the DC field within the drift region, the means for supplying an RF voltage being connected to the rings;

(ii) a multipole rod set including an RF power supply connected to the rod set and means for establishing a potential gradient along the rod set, the means for supplying an RF voltage being connected to the rod set; and

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(iii) a conductive cylinder.

Claim 32 (original): A spectrometer as claimed in claim 29, 30 or 31 wherein the collision cell includes at least one of: a segmented multipole rod set and means for applying varying DC voltages to the multipole rod set, thereby to generate a DC field within the rod set and a potential gradient along the collision cell, to promote travel of ions through the collision cell; and a ring guide comprising a plurality of rings, the collision cell further including an RF power supply for the multipole rod set and the ring guide

Claim 33 (original): A method for separating ions based on ion mobility characteristics, the method comprising:

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- (i) generating ions;
  - (ii) providing a drift region having an axis extending there along;
  - (iii) forming a DC gradient along the drift region;
  - (iv) supplying ions to the drift region, whereby ions are driven through the drift region by the potential gradient, thereby to promote ion separation due to differing ion mobility characteristics;
  - (v) passing the ions into a collision cell to promote at least one of fragmentation and reaction with a collision gas, thereby to generate product ions;
  - (vi) passing the ions through an RF ion guide and maintaining gas at a pressure in the RF guide sufficient to focus the ions along an axis of the RF ion guide; and
  - (vii) subjecting the product ions to mass analysis.

Claim 34 (original): A method as claimed in claim 33, which includes, before step (v), passing the ions through a first mass analyzer, to select a desired precursor ion.

Claim 35 (original): A method as claimed in claim 33 or 34, which includes providing a potential gradient along the collision cell, to promote passage of ions through the collision cell.

Claim 36 (currently amended): A method as claimed in claim ~~33~~ or 34, which includes at least one of: varying the potential gradient along the drift region with respect to time, thereby to vary the rate at which ions elute from the drift region; and providing a non-linear potential gradient along the drift region, whereby the potential gradient at an end of the drift region promotes elution of ions at a desired rate.

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Claim 37 (original): A method as claimed in claim 36, which includes, as different ions elute from the IMS drift region, switching the precursor ions selected by the first mass analyzer to correspond to an ion peak eluting from the drift region, thereby to maximize utilization of ions from a sample and enable sequential analysis of a plurality of different precursor ions present in the sample.

Claim 38 (original): A method of separating ions based on ion mobility characteristics, the method comprising:

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- (i) generating ions;
  - (ii) providing at least one drift region having an axis extending therealong and providing and maintaining a gas at a desired pressure in the drift region;
  - (iii) forming a DC potential gradient along the drift region;
  - (iv) supplying ions to the drift region, whereby ions are driven through the drift region by the potential gradient and ions tend to separate due to differing ion mobility characteristics;
  - (v) passing ions into a mass analyzer for mass analysis in dependence upon ion mass-to-charge ratios; and
  - (vi) adjusting parameters of the mass analyzer to follow changes in properties of ions eluting from the drift region.

Claim 39 (original): A method as claimed in claim 38, which includes separating ions into groups of ions in step (iv) in dependence upon mobility characteristics, and sequentially analyzing each group of ions in step (v).

Claim 40 (original): A method as claimed in claim 38 or 39, which includes mass analyzing the ions in step (v), with a time-of-flight mass spectrometer.

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Claim 41 (new): A method as claimed in claim 33, which includes at least one of: varying the potential gradient along the drift region with respect to time, thereby to vary the rate at which ions elute from the drift region; and providing a non-linear potential gradient along the drift region, whereby the potential gradient at an end of the drift region promotes elution of ions at a desired rate.

Claim 42 (new): A method as claimed in claim 33 wherein the ions undergo steps (v) and (vi) concurrently.

Claim 43 (new): A spectrometer as claimed in claim 29 wherein the collision cell comprises the RF ion guide.